Combining commercial production of multi-products in a GMP environment with Clinical & R&D activities

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Introduction

Mono-product facilities are turning to multi-product to cope with decreasing prices of [^{18}F]-FDG (FDG) and to support R&D programs. The aim is to demonstrate that in the same facility and equipment, a busy research program can be safely integrated into commercial production.

Materials & Methods

To be able to safely combine both activities a risk-assessment should be designed to identify key control points. The use of a fully automated platform (e.g. IBA Synthera) and its disposable cassettes can prevent human errors, reduce risk of cross-contamination and improve reliability. A production schedule, training and labeling procedures should also be considered.

Results

Positronpharma in Chile delivers FDG daily to several hospitals and produced > 1600 Ci FDG in the last 3 years. In addition, [^{18}F]-(FCH, NaF, FET, FLT, F-MISO, DMFP), [^{68}Ga]-DOTA-peptides and PSMA-11 have been implemented as well as two more INDs: [^{18}F]-PR04MZ and MHMZ were translated into clinical studies. ICNAS is a research unit of the University of Coimbra that hosts a GMP-compliant PET production facility which supports clinical and pre-clinical R&D programs and supplies RPs to nearby hospitals. The unit is in operation since 2012 and currently has five radiopharmaceuticals authorized in the market (^{18}F-: FDG, FCH, NaF) and ^{68}Ga-DOTA-NOC. All are produced on IBA Synthera and together represent >2000 production cycles. An extensive R&D program is in place with plans for production of other [^{18}F]-tracers (F-DOPA nucleophilic route, FMISO, FLT, FES), [^{68}Ga]- (PSMA, DOTA-TOC) and [^{64}Cu]- (ATSM). BV Cyclotron VU in Amsterdam is a private company with a GMP-compliant PET production facility. Since the 90's FDG is

delivered for the Dutch hospitals (annual output of > 7300 patient doses (11 TBq)). FCH and FBB (Florbetaben) are also commercially produced with annual output >1400 (1.7 TBq) and >340 patient doses (1.1 TBq), respectively. Besides the commercial productions there is also room for an R&D program, e.g., currently improvement of the production of FCH is examined.

Discussion/Conclusion

As a conclusion, the sites described have been functioning for several years and are able to safely combine commercial daily production while keeping a highly active R&D program with more than ten different tracers developed for pre-clinical and clinical applications.